

CLAIM AMENDMENTS

Claims 1-28 and 32-35 are withdrawn.

29. (amended) A method of identifying a compound which modulates the interaction of GRF4 with Ras, comprising

- a) contacting (i) GRF4 or a portion of GRF4 selected from the group consisting of a Ras association domain and a CDC25-related GEF domain, a Ras-binding fragment of GRF4 or a derivative of either of the foregoing (ii), with (ii) Ras a GRF4-binding fragment of Ras or a derivative of either of the foregoing in the presence of the compound; wherein (i) and (ii) are capable of binding; and
- b) determining whether the binding between (i) and (ii) is modulated compared to a control for determining the binding of GRF4 and Ras in the absence of the compound, thereby wherein an increase or decrease in binding in the presence of the compound indicates indicating that the compound modulates the interaction of GRF4 and Ras.

30. (amended) A method of identifying a compound which modulates the interaction of GRF4 with Rap1, comprising

- a) contacting (i) GRF4 or a portion of GRF4 selected from the group consisting of a Ras association domain or and a CDC25-related GEF domain, a Rap1-binding fragment of GRF4 or a derivative of either of the foregoing with (ii) Rap1, a GRF4-binding fragment of Rap1 or a derivative of either of the foregoing in the presence of the compound; wherein (i) and (ii) are capable of binding; and
- b) determining whether the binding between (i) and (ii) is modulated compared to a control for determining the binding of GRF4 and Rap1 in the absence of the compound, wherein an increase or decrease in binding in the presence of the compound indicates thereby indicating that the compound modulates the interaction of GRF4 and Rap1.

31. (amended) A method of evaluating the cell proliferation reducing properties of a compound comprising contacting the compound with:

- a) (I) GRF4, or a portion of GRF4 selected from the group consisting of a Ras association domain or a CDC25-related GEF domain~~a Ras binding fragment of GRF4 or a derivative of either of the foregoing; and~~
- b) (ii) Ras, - in the presence of the compound~~a GRF4 binding fragment of Ras or a derivative of either of the foregoing; wherein (a) and (b) are capable of binding; and~~
- c) determining whether the binding between (i) and (ii) is modulated inhibited compared to a control for determining the binding of GRF4 and Ras in the absence of the compound, wherein an increase or decrease an inhibition of binding in the presence of the compound indicates the ability of the compound to interfere with the binding of a) with b); the ability to interfere with binding indicating that the compound reduces cell proliferation.

36. (new) The method of claim 29, wherein the GRF4 comprises the following sequence motifs and domains, in amino to carboxyl order: a cyclic nucleotide monophosphate-binding domain, a Ras exchange motif, a PDZ association domain, a Ras association domain, a CDC25-related GEF domain, a first PY motif, a second PY motif, and a COOH-terminal SaV sequence conforming to a PDZ binding motif.

37. (new) The method of claim 29, wherein the GRF4 comprises SEQ ID NO:2 or a sequence of at least 80% sequence identity to SEQ ID NO:2.

38. (new) The method of claim 30, wherein the GRF4 comprises the following sequence motifs and domains, in amino to carboxyl order: a cyclic nucleotide monophosphate-

binding domain, a Ras exchange motif, a PDZ association domain, a Ras association domain, a CDC25-related GEF domain, a first PY motif, a second PY motif, and a COOH-terminal SaV sequence conforming to a PDZ binding motif.

39. (new) The method of claim 30, wherein the GRF4 comprises SEQ ID NO:2 or a sequence of at least 80% sequence identity to SEQ ID NO:2.

40. (new) The method of claim 31, wherein the GRF4 comprises the following sequence motifs and domains, in amino to carboxyl order: a cyclic nucleotide monophosphate-binding domain, a Ras exchange motif, a PDZ association domain, a Ras association domain, a CDC25-related GEF domain, a first PY motif, a second PY motif, and a COOH-terminal SaV sequence conforming to a PDZ binding motif.

41. (new) The method of claim 31, wherein the GRF4 comprises SEQ ID NO:2 or a sequence of at least 80% sequence identity to SEQ ID NO:2.